Amendments to the Claim

1-34. (cancelled)

35. (original) A stable pharmaceutical formulation comprising:

    a) a GLP-1 compound selected from the group consisting of: GLP-1, GLP-1 analogs, and GLP-1 derivatives wherein the GLP-1 compound can bind to the GLP-1 receptor;

    b) a tween polymeric surfactant;

    c) a preservative; and

    d) a buffer

    wherein the stable formulation is a solution and has a pH between about 6.5 and about 9.0.

36. (original) The formulation of Claim 35, wherein the GLP-1 compound is protected from the activity of dipeptidyl-peptidase IV.

37. (original) The formulation of Claim 35, wherein the GLP-1 compound comprises the sequence of SEQ ID NO:1 or SEQ ID NO:4.

38. (original) The formulation of Claim 36 wherein the GLP-1 compound comprises the sequence of SEQ ID NO:5.

39. (amended) The formulation of Claim 35 wherein the GLP-1 compound is GLP-1(7-34), GLP-1(7-35), GLP-1(7-36), GLP-1(7-37), or the amide forms thereof, with at least one modification selected from the group consisting of:

    (a) substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, arginine, or D-lysine for lysine at position 26 and/or position 34 or substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, lysine, or a D-arginine for arginine at position 36;

    (b) substitution of an oxidation-resistant amino acid for tryptophan at position 31;

    (c) substitution according to at least one of:

    Y for V at position 16;

    K for S at position 18;

    D for E at position 21;

S for G at position 22;
R for Q at position 23;
R for A at position 24; and
Q for K at position 26;

(d) substitution comprising at least one of:
glycine, serine, or cysteine for alanine at position 8;
aspartic acid, glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glutamic acid at position 9;
serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glycine at position 10; and
glutamic acid for aspartic acid at position 15; and

(e) substitution of glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine or the D or N-acylated or alkylated form of histidine for histidine at position 7.

40. (original) The formulation of Claim 39, wherein the GLP-1 analog is acylated at an amino acid side group.

41. (original) The formulation of Claim 40, wherein the GLP-1 analog is acylated on the epsilon-amino group of lysine.

42. (original) The formulation of Claim 41, wherein the lysine that is acylated is lysine 34.

43. (original) The formulation of Claim 42, wherein the epsilon-amino group of lysine is acylated with an acyl group selected from the group consisting of C_6-C_{10} unbranched acyl.

44. (amended) The formulation of Claim 35 wherein the GLP-1 ~~molecule~~ compound is a GLP-1 derivative prepared by the process of acylating a GLP-1 analog selected from the group consisting of GLP-1(7-34), GLP-1(7-35), GLP-1(7-36), GLP-1(7-37), and the amide forms thereof, with at least one modification selected from the group consisting of:

(a) substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, arginine, or D-lysine for lysine at position 26 and/or

position 34 or substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, lysine, or a D-arginine for arginine at position 36;

(b) substitution of an oxidation-resistant amino acid for tryptophan at position 31;

(c) substitution according to at least one of:
Y for V at position 16;
K for S at position 18;
D for E at position 21;
S for G at position 22;
R for Q at position 23;
R for A at position 24; and
Q for K at position 26;

(d) substitution comprising at least one of:
glycine, serine, or cysteine for alanine at position 8;
aspartic acid, glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glutamic acid at position 9;
serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glycine at position 10; and
glutamic acid for aspartic acid at position 15; and

(e) substitution of glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine or the D or N-acylated or alkylated form of histidine for histidine at position 7.

45. (original) The formulation of Claim 44 wherein the GLP-1 analog has an arginine substituted for lysine at position 34.

46. (original) The formulation of Claim 45 wherein the GLP-1 analog is acylated on the epsilon-amino group of lysine.

47. (original) The formulation of Claim 35, wherein the GLP-1 compound is a GLP-1 derivative.

48. (original) The formulation of Claim 35 further comprising an isotonicity agent.

49. (original) The formulation of Claim 48 wherein the isotonicity agent is glycerin.
50. (original) The formulation of Claim 48 wherein the isotonicity agent is sodium chloride.
51. (original) The formulation of Claim 35 further wherein the preservative is phenol.
52. (original) The formulation of Claim 35 further wherein the preservative is m-cresol.
53. (amended) A method of treating a person having a condition for which administration of a GLP-1 compound to patients with elevated glucose levels ~~is indicated~~, said method comprising administering a pharmacologically effective amount of a formulation of Claim 35.
54. (new) The method of claim 53 wherein the condition is Type II diabetes.

Claim Objections

The Examiner objected to Claims 39, 44 because of the following informalities: in claim 39, in paragraph (e), after "substitution" and before "glycine," the term -of- should be added. In claim 44, line 2, "molecule" should be cancelled and replaced with – compound- in order to remain consistent with the language of claim 35. Furthermore, in claim 44, paragraph (e), the term –of- should be added after "substitution" and before "glycine." Applicants have amended the claims to address the Examiner's objections.

REJECTION UNDER 35 U.S.C. § 112

The Examiner rejected Claim 53 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicants have amended the claims include the limitation of treating patients with elevated glucose levels. Additionally, Applicants' specification includes disclosure of GLP-1 compounds being useful in treating Type II diabetes, Type I diabetes, having the ability to elicit increased insulin secretion and biosynthesis, to reduce glucagon secretion, to delay gastric emptying, and to preserve and even restore pancreatic beta cell function. (See page 1 lines 13 to 24 of Applicants' specification). The condition to be treated is a patient having elevated glucose levels. Thus, an adequate written description is provided. Applicants respectfully submit that this rejection is inappropriate and request reconsideration and withdrawal of the rejection.

REJECTION UNDER 35 U.S.C. § 103

The Examiner rejected Claims 35-53 under 35 U.S.C. §103(a) as "as being unpatentable over Knudsen et al., 6,458,924." The Examiner previously determined that Knudsen is not prior art because the disclosure of specific surfactants is not supported in the priority application.

> "Knudsen et al (US 2001/0011071) is cited as art of interest. However, Knudsen et al's disclosure of specific surfactants (see, e.g., paragraph 1605) is not supported in the disclosure of Knudsen et al's priority applications serial no. 08/918,810 or PCT/DK97/00340 (= WO Patent Application 98/08871), and accordingly Knudsen et al is not prior art against the instant claims." (See Notice of Allowability, paper

number 16 of Application/Control Number: 09/585,181, by Jeffery Russell, October 20, 2001.)

Therefore, the obviousness rejection is moot because Knudsen is not prior art.

Double Patenting

The Examiner rejected Claims 35-53 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,358,924 in view of Knudsen et el., supra. Likewise, as stated above, Knudsen is not prior art and therefore the rejection is moot.

If the Examiner feels that a telephone conversation with Applicants' Attorney would be helpful in expediting the prosecution of this case, the Examiner is urged to call Applicants' Attorney at (317) 277-2620

Respectfully submitted,

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